Proposed Synopsis on

"Preparation and Characterization of Mesoporous Nanoparticles of Poorly Water Soluble drug candidates and Development of its suitable formulation"

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Abstract:

This study implies the use of mesoporous nanparticles to evaluate the presentation of mesoporous carrier for poorly water soluble drug candidate. Mesoporous nanoparticles selected as a carrier for poorly water-soluble drug candidate. Characterization of mesoporous nanoparticles were carried out by SEM, IR, DSC, and PXRD. The Percent drug release will calculate by in vitro dissolution. As in vitro dissolution is directly associated with bioavailability, a promising approach to boost dissolution is encapsulation of hydrophobic amorphous drug candidate in mesoporous materials. They can be developed by using a comparatively simple process, thus making it cost effective. By controlling the parameters during the synthesis; the morphology, pore size and volume and particle size of mesoporous nanoparticles can be altered consequently.The exceptional features of mesoporous materials, including their highly mesoporous structure, high surface area, large pore volume, tunable pore size, good biocompatibility, and thermal stability have led to these materials becoming important drug carriers. This work concluded that mesoporous nanoparticles therefore be considered as a promising carrier to achieve enhanced water solubility for drugs with low water solubility.

Introduction:

Drug delivery technologies utilizing a variety of carriers have resulted in revolution in the approach towards drug solubility and bioavailability. Due to low solubility of drug molecules resulting less bioavailability, patients have to take high doses of the drug to attain the desired therapeutic effects for the treatment of diseases. To resolve these problems, there is various drug carriers system which can used to deliver active therapeutical agent to the desired site in the body. Hence mesoporous materials are a capable to overcome low solubility problems and produce desired effect. Mesoporous materials have recently paying attention because of their promising applications in drug delivery. Mesoporous nanoparticles are widely used as a delivery reagent that is carrier agent because of its high stability towards chemical properties, thermal stability. The mesoporous nature of material provides greater loading of therapeutic agent and their release of the desired site. The promising properties of mesoporous nanoprticles counting pore size, high drug loading, and porosity are controlled additives added used for preparation of mesoporous nanoparticles.

There are two main stage process first hydrolysis and second one is condensation. The mesoporous nanoparticle , because of the easily synthesis, ease of surface functionalization, tunable pore size, large surface area, and biocompatibility, are being useful in pharmaceuticals drug delivery. It has been a effective nanocarrier for various therapeutic agents. Mesoporous nanoparticles are taken as one of the most capable nanocarriers to perform controlled drug delivery.

Promising characteristics of mesoporous materials having :

1. Highly porous structure of mesoparticles having different pore sizes and shapes.
2. Higher surface areas which facilitate them for sorption processes.
3. Their pore size distribution is usually very pointed and it is dependent on surfactant usd.
4. Different shape and structure of materials are obtained by utilizing different surfactant.

Review of literature:

1. Magdalena Prokopowicz et al; (2020) had reported new biphasic composites of calcium phosphate and mesoporous silica material in the form of powders and pellets as a potential bone drug delivery system for doxycycline hydrochloride Biphasic composite of calcium phosphate-based mesoporous silica as a novel bone drug delivery system. The cytotoxicity assays demonstrated that the calcium phosphate content in mesoporous silica increases osteoblasts viability indicating the calcium phosphate content in mesoporous silica (30% CaP content) as the most biocompatible. The obtained biphasic calcium phosphate content in mesoporous silica composites seem to have an application potential as bone-specific drug delivery system.

2. Gosavi A A et al; (2021) had reported SBA-15 MSN of Luliconazole. Its molecular size was suitable for incorporation in to the mesoporous of the SBA-15 materials. The SBA-15 was characterized by FTIR, UV analysis, Particle size, Transmission electron microscopy. The results revealed that prepared mesoporous silica have small particle size, high surface area, and enhanced drug dissolution rate. The results obtained showed that Luliconazole was loaded with great efficiency into the SBA-15 which leads to enhanced diffusion of drug. Luliconazole hydrogel formulations improved medication permeation across the skin appropriate polymer was used to produce the formulation (Carbopol 934p and HPMC). The physiochemical parameters of all the established luliconazole formulations were assessed, including gel appearance, pH, viscosity, spreadability, globule size, Zeta potential, and drug content.

3. Lakshminarasimhan Harini et al; (2019) had reported an ingenious non-spherical mesoporous silica nanoparticle cargo with curcumin induces mitochondria-mediated apoptosis in breast cancer (MCF-7) cells. Non-spherical mesoporous silica nanoparticle coated with PEI was characterized for its drug delivery efficiency in MCF-7 cells. The non-spherical shape of MSNAP synthesized by origami method aids reduction in toxicity, faster intracellular accumulation, and better drug release. Drug released from MSNAP intracellularly even at lower

concentration disturbs the cellular organelles and induce apoptosis. Additionally, MSNAP mediated drug delivery sensitized resistant cells at subordinate drug concentration. Also he had reported the mesoporous silica nanoparticle with non-spherical shape has to influence on cytotoxicity and drug delivery.

4. Jadhav et al.; (2021) had reported Tamoxifen mesoporous nanoparticles. Tamoxifen is a BCS class II drug which is having problem with solubility. FDT (fast dissolving tablet) is used to achieve immediate action of drug and to avoid first pass metabolism API reaches to site of action. Both nanoparticles and FDT resulted in increased solubility and immediate action which results is increased bioavailability

5. Prajakta Tambe et al; (2018) had reported decapeptide-conjugated MSNPs loaded with DOX for the targeted drug delivery in breast and prostate cancer cells. MSNPs showed excellent porous structure and loading of DOX higher uptake of DOX-loaded targeted MSNPs was observed. The targeted MSNPs also showed significantly higher cytotoxicity than DOX-loaded bare MSNPs at different time points. Her study suggested GnRH analog-conjugated targeted MSNPs can be the suitable and promising approach for targeted drug delivery in all hormone-dependent cancer cells.

6. Mohit Mahajan et al; (2018) had reported development of mesoporous silica nanoparticles of ritonavir with enhanced bioavailability potential: formulation optimization, in-vitro and in-vivo evaluation. RTV was loaded in both the silica nanoparticles to examine the effect on solubility through the drug loading. The characterization results like DSC, PXRD and N_2 adsorption-desorption confirmed that the RTV was successfully loaded into the mesoporous silica nanoparticles . Both MCM-41NPs and MCM-48NPs showed several advantages as a carrier for drug delivery respectively. Both MCM-41NPs and MCM-48NPs could notably increase the dissolution rate of RTV as compared to the pure RTV, but R- MCM-48NPs showed better in the fast release.

7. S. Sharmiladevi et al; (2016) had reported synthesis of mesoporous silica nanoparticles and drug loading for gram positive and gram-negative bacteria. Antibacterial activity of mesoporous silica nanoparticles and tetracycline loaded mesoporous silica nanoparticles was carried out using tetracycline as a positive control for gram-positive (Staphylococcus aureus) and gram negative (Escherichia coli) bacteria. The antibacterial studies suggest that the mesoporous silica nanoparticles can be used as potential drug candidature to treat various diseases.

8. Thashini Moodley et al;(2019) had reported MSN loaded 5-FU formulations. The 5-FU release from MSN without triggering systemic toxicity in healthy tissue or accumulation in non-targeted organs. MSN is a relatively biodegradable material that has been commercially and clinically applied as additives in a variety of products with no adverse toxicities noted. Thus, an oral administration of 5-FU would be highly advantageous, as the matrix is capable of sustained drug release.

Objectives of Research

In the present study is aimed as.

Aim

"Preparation and Characterization of Mesoporous Nanoparticles of Poorly Water soluble drug candidates and development of its suitable formulation"

Objectives

1. To synthesized mesoporous nanoparticles of the selected drug candidate using appropriate approach.

2. To carry out characterization of mesoporous nanoparticles.

3. To make an effort to load the drug candidate into the mesoporous nanoparticles.

4. To make an effort to develop a suitable formulation of mesoporous nanoparticles and its characterization.

5. To perform *In-vitro* study of developed formulation.

6. To perform Stability study of finished formulation.

7. To perform *In-vivo* study of finished formulation.

Methodology to be adopted

1. Thorough Literature survey

Literature survey will carried out as per the study design needs and to adopt appropriate techniques for present work. Reverse literature survey during work will be also considered if needs.

2. Selection of Drug, Excipients and Chemicals

On the basis of literature survey the selection of therapeutic category and there by drug, various excipients, and chemicals will be selected for the proposed mesoporous nanoparticles.

3. Procurement of Drug, Excipients and Chemicals

The selected drug, polymers and various chemicals will be procuring from different manufacturer by buying or requesting them for free gift samples for the purpose of research.

4. Preformulation Study

Preformulation study like determination of appearance, melting point, solubility will be carry out by official or reference standard methods. The determination of standard wavelength, preparation of calibration curve will be carried out by using UV spectroscopy or HPLC or various reference standard analytical methods. Drug polymer interaction study will be carried out by IR study.

5. Preparation of mesoporous nanoparticles.

Mesoporous nanoparticles will be prepared by various reference methods on trial and error basis. The appropriate method will be selected for the preparation of mesoporous nanoparticles.

6. Drug loading into mesoporous nanoparticles.

The drug candidate will load into mesoporous nanoparticles bu using appropriate method.

7. Characterization mesoporous nanoparticles.

The prepared mesoporous will be evaluated for its Particle size, Drug entrapment efficiency. Differential Scanning Caloriemetry (DSC), Surface topography (SEM) etc.

8. To formulate suitable formulation of mesoporous nanoparticles and its characterization.

After the synthesis of mesoporous nanoparticles an approach to formulate suitable formulation of mesoporous nanoparticals will carried out. Characterization of finished product will carried out.

9. *In- Vitro* study of developed formulation.

The develpoed formulation will be subjected to *In-Vitro* study

10. Stability study

The finished formulation of mesoporous nanoparticles will be subjected to further stability study.

11. *In-Vivo* study of finished formulation.

The finished formulation will be subjected to *In Vivo* Pharmacokinetic study.

12. Interpretation of data

The obtained data from the various performed experiments will be fitted to desired statistical analysis and same will be the presented.

Rationals of study:

The formulation development of low solubility drugs (BCS class II and IV) faces a great challenge as these drugs are poorly absorbed and usually exhibit subsequent low or variable oral bioavailability. Mesoporous materials effective for drug amorphisation due to their ability to achieve the spatial confinement of drug molecules within their nanometre-scale pore structure suggested that drugs would exist in an amorphous state within the mesoporous material if the pore size were smaller the drug's molecular size. Due to the spatial confinement of drug molecules within the mesoporous network, low solubility crystalline drugs can be converted into their amorphous counterparts, which exhibit higher solubility. Mesoporous nanoparticles gives extensively environment to drug candidate without change its form. Mesoporous carriers also prevent nucleation resulting that prevent crystallization. Mesoporous carriers having also flexibility due to tunable pore size and surface area. Mesoporous carriers accelerate dissolution and impart in high bioavability to enhance the bioavailability of poorly soluble drugs.

Proposed Work Plan:

The research work was proposed to proceed as follows:

1. Thorough literature survey
2. Selection of drug candidates, excipients and excipients.
3. Procurement of drug candidates, excipients and chemicals.
4. Preformulation study
   - Appearance
   - Melting point
   - IR analysis
5. Preparation of mesoporous nanoparticles.
6. Loading of therapeutic agent into mesoporous nanoparticles
7. Characterization of drug loaded mesoporous nanoparticles
   - Surface topography (SEM)
   - % yield
   - Drug entrapment efficiency
   - IR study
   - Differential scanning caloriemetry (DSC)
   - Powder X ray diffraction analysis.
8. To develop Suitable formulation of Mesoporous Nanoparticals.
9. *In –Vitro* study

   To perform *In –Vitro* study of developed formulation.
10. Stability study of finished formulation.
11. *In-vivo* study
    - To perform *In-vivo* Pharmacokinetic study of finished formulation.

Interpretation and presentation of data**.**

Probable outcome:

Probable outcome of the study will be as follows;

1. The Mesoporous Naoparticles may form with desired porosity with desired surface characteristics.

2. The Drug candidate may be loaded in greater extent into the mesoporous nanoparticles carriers.

3. The Characterization of Mesoporous Nanoparticles may show desired characterized parameters.

4. The suitable formulation of Poorly water soluble drug candidate with Mesoporous Nanoparticles may be developed.

5. The Evaluation parameters of developed formulation of Mesoporous Nanoparticles may show desired result.

6. Mesoporous Nanoparticles carriers may be proven excellent alternatives to address the issue of poor water solubility of drug without any significant alteration of drug candidate.

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